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METHODS & REVIEWS

Biotechnology Core Laboratories: An Overview

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An assessment of the capabilities of biotechnology core facilities requires access to current data on state-of-the-art technologies, personnel, space, services, financial issues, and the demand for such facilities. Data on these topics should be useful to researchers, facility personnel, administrators, and granting agencies. To obtain such data, the Association of Biomolecular Resource Facilities (ABRF) conducted a general survey on the operation and technical capabilities of core facilities. A total of 81 ABRF core laboratories voluntarily responded to the survey. Just over 60% of the respondents were from academic institutions, with the remaining located in research institutes, industry, and one U.S. government laboratory. Fifty laboratories provided financial data, with 47 of these operating on a nonprofit basis. Four laboratories were fully self-supporting from user fees. A typical facility had three full-time staff members and occupied approximately 1100 square feet (ft^2). The most frequently offered services were N-terminal protein sequencing, protein fragmentation, peptide synthesis and purification, amino acid analysis, DNA synthesis, and DNA sequencing. One third of the facilities provided mass analysis by matrix-assisted laser desorption and ionization (MALDI) mass spectrometry, a recently introduced service that has been offered on an average for 3 years. Another relatively new service, bioinformatics support, is offered by about one third of the responding laboratories. (J Biomol Tech 2000;11:1–11)

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One aspect of the mission of the Association of Biomolecular Resource Facilities[1] (ABRF) is to promote and support resource facilities and their interactions with research laboratories. A profile of biotechnology resource laboratories may be useful in the creation of new core facilities, as well as in the redefinition of the operation of established facilities. This report is the fourth in a series of surveys[2–4] conducted by the Survey Committee of the ABRF to provide information on the changing face of biotechnology core facilities. Topics covered in this survey include details about personnel, space requirements, services offered, number of research laboratories served, sample throughput, charges, cost recovery, and funding issues. Current trends in core facilities have been identified by comparison with the results of the last general survey, which was conducted in 1992.[4]

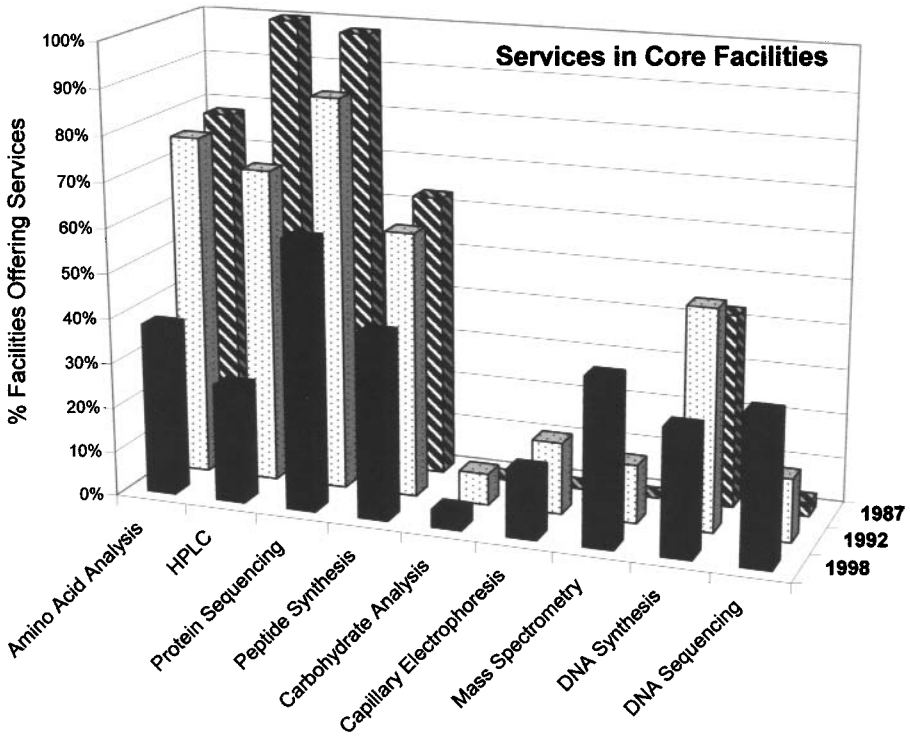

FIGURE 1

Comparison of the percentage of reporting core facilities offering selected services in 1998, 1992, and 1987. Data are taken from results of this survey and earlier surveys.[2,4]

EXPERIMENTAL METHODS

The six-page questionnaire for this survey was posted in January of 1998 on a website established by Lisa Bibbs and Jose Gutierrez of The Scripps Research Institute. Directors of ABRF core facilities were notified of the survey by United States mail and by email through the ABRF electronic discussion group (abrf@aecom.yu.edu). To provide anonymity for responses to the survey, respondents obtained a unique identifier code from Gutierrez. Laboratories wishing to respond electronically through the website submitted each of the six pages of the survey as they were completed. Respondents who preferred to submit a written response were provided with a paper copy of the survey. Eighty-one data sets were collected, with the last data set received in June of 1998.

Data entries that appeared to be inconsistent were clarified if possible by contacting the facility through Gutierrez. The sample size (N), mean, median, and standard deviation (SD) were calculated for each data set. The range includes all of the values reported by facilities with the exception of the outliers. Outliers were defined as data points that differed from the mean by more than four times the standard deviation and were removed from the data sets. In some cases, respondents did not answer all questions in the survey; this is reflected in the sample size. Data sets that had a sample size of less than or equal to 4 were not included in the tables or in the statistical analysis. Student's *t* test for unpaired data was used to determine the statistical significance of differences between means. A significant difference was taken to be $P < 0.01$, with $P < 0.05$ as a probably significant difference. A copy of the survey is available from the corresponding author. Preliminary results from this survey were presented as a poster at the ABRF '99 meeting entitled *Bioinformatics and Biomolecular Technologies: Linking Genomes, Proteomes and Biochemistry*, held March 19 through 22, 1999, in Durham, North Carolina.

RESULTS AND DISCUSSION

Technical Capabilities of Biotechnology Facilities

A very different profile of services offered by a typical facility was seen in 1998, compared with the previous major surveys in 1987[2] and 1992[4] (Fig. 1). The most striking difference seen in Figure 1 is the decrease in the percentage of facilities offering each service, with the exceptions of capillary electrophoresis, DNA sequencing, and mass spectrometry. In 1998, the most commonly offered services (Table 1) were protein sequencing (62%), protein fragmentation (44%), peptide synthesis (42%), amino acid analysis (39%), synthetic peptide purification (38%), DNA sequencing (37%), and DNA synthesis (37%).

TABLE 1

Services Offered in 1998 and the Number of Years Offered

Service	N	Years Median	Mean	SD	Range
DNA services					
DNA synthesis 1–4[a]	29	11	10.5	2.8	4–14
DNA synthesis high[b]	6	2	4.1	5.4	1–15
DNA oligo purification	15	10	8.7	4.2	3–15
Template prep	6	2	3.6	4.0	1–11
DNA sequencing	29	6	5.7	2.9	1–10
Microsatellite analysis	11	1	2.1	1.8	1–6
Protein services					
N-terminal protein seq	49	10	10.3	4.6	1–24
SDS–PAGE	18	8.5	8.6	4.0	3–20
2D gels	10	1.5	2.9	3.1	1–10
Fragmentation	35	7	7.3	4.9	1–20
Peptide synthesis 1–3[c]	33	9	8.6	3.5	1–14
Peptide synthesis high[d]	11	6	6.4	3.9	1–15
Peptide purification	30	9	8.6	3.6	1–15
Amino acid analysis	31	12	12.2	6.1	4–30
CE[e]	12	5	4.6	2.2	1–8
HPLC[f]	21	8	8.1	4.9	1–20
Mass spectrometry[g]					
MALDI (mass)	26	2.5	2.7	1.8	1–8
MALDI (sequence)	5	2	1.8	0.8	1–3
Electrospray (mass)	16	4	3.7	2.4	1–8
Electrospray triple quad	11	4	4.0	2.4	1–8

[a]DNA synthesis 1–4: synthesis with a 1 to 4 column instrument.
[b]DNA synthesis high: synthesis with a >4 column instrument.
[c]Peptide synthesis 1–3: synthesis with an instrument with up to three reaction vessels.
[d]Peptide synthesis high: synthesis with an instrument with more than 3 reaction vessels.
[e]Capillary electrophoresis.
[f]High performance liquid chromatography.
[g]Subcategories of mass and sequence were defined for MALDI and mass for electrospray with the second category not defined to accommodate multiple uses.

In 1992, the distribution of facilities offering these services was as follows: protein sequencing (87%), protein fragmentation (31%), peptide synthesis (59%), amino acid analysis (76%), DNA sequencing (14%), and DNA synthesis (49%).

The percentage of laboratories offering mass spectrometry has tripled since 1992, and the percentage offering DNA sequencing has more than doubled. Amino acid analysis, carbohydrate analysis, and high-performance liquid chromatography (HPLC) services have dropped by more than one half since 1992. The remaining services are currently offered by approximately the same percentage of laboratories as reported in the 1992 survey. New services that have been added since 1992 include high-throughput DNA synthesis, DNA template preparation, microsatellite analysis, C-terminal protein sequencing, two-dimensional (2D) gel electrophoresis, bioinformatics, and all categories of analysis by mass spectrometry.

The service that has been offered for the longest average period (12 years) was amino acid analysis. DNA synthesis with a 1- to 4-column instrument (Table 1, *footnote a*) and N-terminal protein sequencing were the next oldest services, with 10 years each. Services that have been offered for 5 to 9 years include DNA oligonucleotide purification, DNA sequencing, sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS-PAGE), protein fragmentation, peptide synthesis, peptide purification, carbohydrate analysis, and HPLC.

Survey participants were asked to provide information regarding bioinformatics services offered by

TABLE 2

Number of Samples per Month

Service	N	Median	Mean	SD	Range
DNA services					
DNA synthesis 1–4	28	200	244	244	20–1218
DNA synthesis high	6	688	697	508	80–1327
DNA oligo purification	14	45	74	66	3–180
Template prep	5	100	215	329	5–800
DNA sequencing	28	900	1176	1096	169–5000
Microsatellite analysis	11	100	641	1466	10–5000
Protein services					
N-terminal protein seq	49	17	27	25	3–120
SDS–PAGE	16	2	4	6	1–25
2D gels	8	6	8	8	1–20
Fragmentation	34	4	13	19	0.1–91
Peptide synthesis 1–3	35	9	10	8	0.5–35
Peptide synthesis high	11	15	19	13	5–40
Peptide purification	31	5	8	9	0.3–35
Amino acid analysis	28	24	63	80	0.3–300
Mass spectrometry					
MALDI (mass)	25	50	163	254	5–1000
MALDI (sequence)	5	1	12	22	0.5–50
Electrospray (mass)	16	45	322	983	10–4000
Electrospray triple quad	12	18	44	58	0.5–200

their laboratories. Bioinformatics, defined here in its broadest sense, can range from simple database searches to complex molecular modeling. Of the 81 responding facilities, 32% offered some form of bioinformatics services. Of these, 62% had dedicated bioinformatics support staff, and 88% had dedicated space, averaging 84 ft^2. Only three of the 26 laboratories charged for this service, and only 10 facilities offered training in the use of bioinformatics resources.

Facilities were asked to report other services that they provide beyond those listed in the survey. HPLC protein purification was offered by two laboratories. Circular dichroism was also offered by two laboratories. Fermentation, fluorescence spectroscopy, optical biosensor studies, modeling, imaging, genechip microarray technology, and quantitation by real-time polymerase chain reaction (PCR) were each mentioned once as other services offered by the respondents demonstrating the breadth of technologies implemented in core facilities.

According to survey results, 10 (12%) of the responding facilities from industry, research institutes, and academic institutions performed some services under Good Lab Practices (GLP) guidelines. GLP standards for amino acid analysis were offered by four laboratories, and five did so for protein sequencing. Two offered GLP services for DNA synthesis, two for DNA sequencing, two for peptide synthesis and purification, and three for electrospray mass spectrometry. Carbohydrate analysis, capillary electrophoresis, 2D gel electrophoresis, and HPLC were all mentioned once as offered under GLP guidelines.

Productivity of Core Facilities

Among individual services, there was a wide range in sample throughput per month (Table 2). The data also show that there was a wide range in throughput reported by the responding laboratories for any one service. This can be seen in the large standard deviations and ranges that are reported. Automated DNA sequencing (1180 ± 1100 samples/month) had the highest throughput on average, followed by high-throughput DNA synthesis (700 ± 510) and microsatellite analysis (640 ± 1470). The lower throughput for synthetic DNA purification (74 ± 66) may reflect the fact that most synthetic oligonucleotides do not need purification.

The number of instruments per service ranged from one to eight, with most laboratories reporting one or two instruments per service. On average, the services (which typically had two instruments) included low-throughput DNA synthesis, DNA

sequencing, protein sequencing, SDS-PAGE, 2D gels, protein fragmentation, and synthetic peptide purification. The remaining services had an average of one instrument.

With regard to the number of cycles per month (eg, the number of base additions in DNA synthesis), high-throughput DNA synthesis had the highest average at 19,000 cycles per month, followed by low-throughput DNA synthesis (5200 cycles). N-terminal protein sequencing and peptide synthesis ranged from 150 to 400 cycles.

The services with the fastest delivery (Table 3) or turnaround time (<3 days) were DNA-related services, including high- and low-throughput DNA synthesis, synthetic DNA purification, DNA sequencing, and template preparation. Somewhat longer turnaround times of 4 to 6 days were reported for microsatellite analysis, N-terminal protein sequencing, amino acid analysis, and SDS-PAGE. The longest turnaround times, ranging from 8 to 14 days, were for protein services, including protein fragmentation, 2D gels, and peptide synthesis (high and low throughput), and peptide purification.

The amount of time spent by responding laboratories on applications that were not directly related to customer services, including experiments performed to standardize instruments and methods development, could be categorized into three distinct groups: low (<6%), intermediate (14% to 30%), and high (>30%). In general, the low group was made up of DNA services (including DNA synthesis, oligonucleotide purification, template preparation, DNA sequencing, and microsatellite analysis), peptide synthesis and purification, and capillary electrophoresis. The intermediate group included several protein-based services: N-terminal protein sequencing and HPLC (15%) and electrospray (mass) mass spectrometry (18%). Amino acid analysis, protein fragmentation, SDS-PAGE, and 2D gel electrophoresis all required 25% to 30% of instrument time. The group that generally required the most time for nonuser runs was in the area of mass spectrometry, MALDI (mass), MALDI (sequencing), and electrospray (triple-quad) mass spectrometry.

The number of principal investigators using an individual service ranged from 1 to 400 (Table 4).

TABLE 3

Turnaround Time

	Days				
Service	N	Median	Mean	SD	Range
DNA services					
DNA synthesis 1–4	28	2	2.1	0.8	1–4
DNA synthesis high	6	1.5	1.6	0.4	1–2
DNA oligo purification	14	2	2.5	1.9	0.5–7
Template prep	6	2	2.8	1.7	1–5
DNA sequencing	30	2	2.8	1.4	1–7
Microsatellite analysis	11	2	3.8	3.9	1–14
Protein service					
N-terminal protein seq	49	4	5.1	4.3	1–21
SDS-PAGE	16	3.5	4.3	3.5	1–15
2D gels	7	10	12.4	9.3	5–30
Fragmentation	33	10	9.5	5.2	1–21
Peptide synthesis 1–3	35	14	14.	8.3	3–35
Peptide synthesis high	11	7	8.0	4.9	2–15
Peptide purification	29	7	8.7	6.8	2–30
Amino acid analysis	30	5	6.0	5.2	0.5–21
CE	10	2	4	6	1–21
HPLC	15	3	5	5	1–21
Mass spectrometry					
MALDI (mass)	25	2	2.5	2.2	1–10
MALDI (sequence)	5	3	5.2	5.1	2–14
Electrospray (mass)	16	3	4.9	5.6	1–21
Electrospray triple quad	12	5	7.4	4.8	3–15

TABLE 4

Principal Investigators Using Each Service per Facility

Service	Principal Investigators				
	N	Median	Mean	SD	Range
DNA services					
DNA synthesis 1–4	27	60	93	101	12–400
DNA synthesis high	6	95.5	155	126	50–367
DNA oligo purification	13	25	65	107	1–400
Template prep	5	5	72	108	1–250
DNA sequencing	29	70	100	94	3–400
Microsatellite analysis	11	4	5.1	4.4	1–16
Protein services					
N-terminal protein seq	46	20	28	21	3–108
SDS-PAGE	16	7.5	11	9	3–35
2D gels	9	7	9	8	1–30
Fragmentation	31	10	13	13	1–50
Peptide synthesis 1–3	34	20	21	13	1–57
Peptide synthesis high	11	30	31	29	5–89
Peptide purification	31	17	20	19	1–78
Amino acid analysis	29	19	27	34	1–175
CE	11	4	32	75	1–250
HPLC	18	5.5	18	40	2–170
Mass spectrometry					
MALDI (mass)	24	15	34	55	1–250
MALDI (sequence)	5	3	13	17	1–40
Electrospray (mass)	14	17	31	33	5–122
Electrospray triple quad	11	20	99	242	5–824

In this survey, a principal investigator was defined as the head of a laboratory, so that several clients from the same laboratory would not be individually counted. The greatest number of principal investigators on average were reported for high-throughput DNA synthesis (154), low-throughput DNA synthesis (93), DNA sequencing (101), and triple-quad electrospray mass spectrometry (99).

Comparing the number of principal investigators using each service in 1998 to 1992, the largest increases were seen in capillary electrophoresis (20-fold), DNA sequencing and template preparation (6-fold), HPLC (4-fold), and low-throughput DNA synthesis and peptide purification (2-fold). The average number of principal investigators did not decrease between 1992 and 1998 for any service.

Staffing and Space Requirements of Core Facilities

The average core facility in 1998 had 3.1 full-time personnel. In 1992, 4.1 full-time personnel were reported,[4] and in 1987, about three full-time personnel were reported.[2] In general, in 1998, a facility had a director plus two full-time and one part-time staff members. In a typical facility, approximately 25% of the staff had a Ph.D. degree, 21% had a master's degree, 33% had a bachelor's degree, and 21% had another degree. In 1987, a typical facility reported that 25% of the staff had a Ph.D. degree, 21% had a master's degree, 50% had a bachelor's degree, and 5% or less had another degree.

In 1998, 54 of the 81 reporting facilities were made up of staff with one director, all of whom worked on providing services. In seven facilities, no director was reported. In four facilities, more than two directors were reported, each in charge of different services. Another eight facilities were made up of only one director, each with no other staff. Assessing how directors spend their time showed that directors in eight facilities did only administrative work and did not work directly on services. In 41 of the 81 reporting facilities, directors reported spending 27% of their time on N-terminal protein sequence analysis. The other most common services on which directors

TABLE 5

Full-Time Staff Requirements for Each Service

Service	N	Mean	SD
DNA services			
DNA synthesis	29	1.01	1.02
Template prep	7	0.52	0.61
DNA sequencing	30	1.25	0.92
Microsatellite analysis	10	0.45	0.59
Protein services			
N-terminal protein seq	36	0.59	0.52
Protein sample prep	29	0.53	0.64
Peptide synthesis	34	0.79	0.66
Amino acid analysis	27	0.49	0.59
CE	8	0.33	0.68
Mass spectrometry	31	0.81	0.74
Administration	32	0.50	0.66
Other	14	0.81	1.02

worked were protein sample preparation (26 facilities), mass spectrometry (25), DNA sequencing (23), and peptide synthesis (23). On average, directors spent 75% of their time in the laboratory or on laboratory-related issues and 25% of their time on administrative work.

Services with the highest number of full-time staff (Table 5) were DNA sequencing (1.25) and DNA synthesis (1.0). Services that required 0.6 to 0.9 staff included peptide synthesis, mass spectrometry, and protein sequencing. Protein sequence sample preparation, DNA template preparation, amino acid analysis, microsatellite analysis, capillary electrophoresis, and administration each employed 0.3 to 0.5 staff members. Services that had the most part-time assistants (50%) included peptide synthesis and DNA sequencing. Other services had part-time assistance in the 20% to 30% range.

The average total space occupied by a core facility is 1090 ft^2 (Table 6), which is not significantly greater than the 959 ft^2 reported in the 1992 survey. This space is used for instrumentation, sample preparation, office, and consultation. A number of services received increased space allocations compared with 1992.[4] These included a 1.8-fold increase in space for DNA sequencing and a 1.6-fold increase in mass spectrometry space. Space allocated to peptide synthesis increased 55%, and space allocated to DNA synthesis increased 26%. Apparently, those laboratories that continue to provide DNA synthesis and peptide synthesis have become larger perhaps because smaller ones have stopped offering these services.

The remaining services remained unchanged or experienced declines in space allocation. Space allocated to carbohydrate analysis, capillary electrophoresis, and amino acid analysis all declined (60%, 32%, and 14%, respectively). The amount of office space remains, on average, 171 ft^2. Consultation space declined from 93 ft^2 in 1992 to 73 ft^2 in 1998, and support space averaged 139 ft^2. The "Other" category averaged 370 ft^2 and included the wide range of nonstandard uses listed in the section on Technical Capabilities (eg, fermentation, solution interactions), as well as cold rooms, hoods, and storage.

This survey also included questions regarding space allocated to a number of new services including DNA template preparation (135 ft^2), protein sequence sample preparation (106 ft^2), microsatellite analysis (111 ft^2), and bioinformatics (84 ft^2).

Core Facility Finances: Income and Expenses

Balancing operational expenses and funding sources is critical to the service level that a facility can provide its users. Fifty of the responding laboratories provided some financial data, and of these, 47 provided information on income and 48 on expenditures. Thirty-five of the responding laboratories were from academia,

TABLE 6

Space Requirements for Services

	Square Feet			
Service	N	Mean	SD	Range
DNA services				
DNA synthesis	32	188	242	6–1000
Template prep	10	135	200	6–588
DNA sequencing	32	288	260	32–117
Microsatellite analysis	8	111	114	4–352
Protein services				
N-terminal protein seq	54	173	202	20–1250
Protein sample prep	44	106	94	2–500
Peptide synthesis	37	248	218	7–1000
Amino acid analysis	36	104	93	10–500
Mass spectrometry	31	254	279	20–1250
Miscellaneous				
Office	71	171	158	16–887
Consultation	15	73	56	20–200
Support	67	158	139	4–720
Other	25	307	370	10–1580
Average total area per lab	79	1091	885	100–4750

TABLE 7

Overall Operating Expenses

Expense	Thousands of U.S. Dollars				
	N	Median	Mean	SD	Range
Supplies/reagents	40	50.0	99.1	93.5	9.2–350.0
Service/repairs	39	16.4	22.9	19.1	2.0–88.0
Depreciation	6	30	34.8	23.9	10.0–70.0
Salaries	39	104.0	138.5	103.0	1.0–28.0
Professional development	25	2.2	4.1	3.5	1.0–15.0

13 from research institutes, 11 from companies, and 1 from government. The data from nonprofit laboratories (ie, universities, research institutions, and government) were pooled for statistical purposes. Because there were few responses from industry, these data were not sufficient for statistical analysis, and the data are not given in the tables.

The overall operating expenses from 41 nonprofit laboratories averaged $257,800 ± $182,500 (median, $177,700) and ranged from $55,000 to $641,000. The overall operating expenses, broken down into subcategories, are detailed in Table 7. A comparison with data from the 1992 survey[4] revealed that only the total figure of $257,800 for overall operating expenses, not the totals for individual categories, was significantly different ($P = 0.001$).

Income to cover operating expenses is obtained by core laboratories from several different sources, including user fees, federal grants, grants from nonfederal sources, and institutional support. Total income was $293,470 ± $228,510 (median, $225,000; minimum, $10,000; maximum, $998,000). This was not significantly different from the 1992 survey finding.

User fees accounted for an average of $151,000 of income. Nine of the laboratories reported that they recover 100% of their costs from user fee income. However, from our recalculations based on the information furnished in the survey, it appears that only four of the nine actually recover all of their costs from user fee income, which ranged from $170,000 to $398,000. Of the laboratories at full recovery, all but one, which was exclusively a DNA sequencing laboratory, offered protein sequencing, three offered some type of mass spectrometry, and one offered no DNA services. This contrasts with the findings in 1992, when the two laboratories that recovered all of their costs from user fees were predominantly DNA-oriented facilities. Among all of the respondents, user fee income ranged from $170,000 to $860,000, which in some cases was not all of the income but at least covered the amount reported for total expenses (excluding instrumentation). Expenses ranged from $150,000 to $865,000 (one outlier of $2,174,000 was excluded from the data set).

Seventeen facilities of the 47 respondents were partially supported from federal grants. Fifteen of these facilities received an average of $75,700 ± $46,800 (median, $77,000) for noncapital expenses, such as reagents and salaries. Ten of the facilities also obtained federal funding for capital equipment, averaging $181,500 ± $159,000 (median, $130,000), ranging between $30,000 and $500,000. This shows federal support for instrumentation in core facilities, probably through instrumentation acquisition granting programs. Only five facilities reported grant funds from nonfederal sources.

Thirty-two core laboratories of the 47 received institutional support. Of these, 31 received support for operating expenses averaging $116,300. Twelve laboratories also received institutional support for capital equipment averaging $112,200. Six laboratories reported income from the Howard Hughes Medical Institute (HHMI). Three received HHMI support for their general operating budgets (primarily salaries), and all six received funds for capital equipment (average, $117,500 ± $110,900; median, $157,600). Nine laboratories received funding from diverse other sources; six of these were for operating expenses averaging $141,600 ± $79,800 (median, $145,000) and three for capital equipment.

The amount of income generated by user fees for any service depends on sample through-put and charges for the services. Sixty-nine of the responding laboratories provided information on charges for one or more services offered. Academic (43) or research institute (14) facilities made up the bulk of the respondents, with the remainder being companies (3) and a government facility (1). Eight respondents did not specify their type of facility. Table 8 shows the range of in-house charges for services across all facilities. The highest flat-rate charges were for MS/MS protein sequencing

TABLE 8

In-House Charges for Services

Service	Setup Charges (Dollars)					Per-Cycle Charges (Dollars)				
	N	Median	Mean	SD	Range	N	Median	Mean	SD	Range
DNA services										
DNA synthesis										
40–50 nmol	7	5.0	6.6	3.2	4–12	24	1.0	1.0	0.3	0.2–1.5
0.2 μmol	9	7.0	7.8	3.5	4–14	25	1.5	1.6	0.5	0.8–2.7
DNA oligo purification										
40–50 nmol	13	10	17	13	1–50					
0.2 μmol	19	15	21	18	2–60					
Template prep	5	7	12	13	4–35					
DNA sequencing	29	15	16	8	2–37					
Microsatellite analysis	8	2.5	6.6	7.6	2–24					
Protein services										
N-terminal protein seq										
<500 fmol	12	82	121	127	30–500	14	15	17	11	4–37
>500 fmol	36	86	104	85	10–500	42	12	16	12	3–62
SDS PAGE	10	58	81	64	16–220					
2D gels	6	138	178	168	46–500					
Fragmentation	26	150	198	177	10–750					
Peptide synthesis										
5–25 μmol	10	79	102	90	25–315	16	12	13	6	1–25
0.1 mmol	13	75	104	125	25–500	20	20	21	10	9–41
0.25 mmol	16	100	142	111	25–450	25	30	35	18	10–90
Peptide purification										
5–25 μmol	12	125	133	109	23–300					
0.1 mmol	16	100	135	94	23–300					
0.25 mmol	19	150	138	93	23–300					
Amino acid analysis	24	32	39	22	11–97					
HPLC	18	50	79	74	8–250					
Mass spectrometry										
MALDI (mass)	20	25	31	20	8–85					
Electrospray (mass)	12	40	52	42	20–180					
MS/MS protein seq	6	125	223	222	40–500					

($223/sample), protein fragmentation and isolation ($198), 2D gels ($178), and peptide purification ($135). The least expensive services included DNA template preparation ($12) and microsatellite analysis ($6.60). DNA sequencing cost about $16 per sample.

Many facilities assessed set-up fees as well as per-cycle fees for peptide synthesis, N-terminal Edman protein sequence analysis, and DNA synthesis. The total charges (set-up and per cycle fees) varied considerably across facilities. For example, synthesis of a 25-mer peptide at the 5- to 25-μmol scale ranged from $50 to $765, with an average of $351. Likewise, synthesis of a 25-mer oligonucleotide at the 40- to 50-nmol scale varied from $8 to $38, with an average cost of $27. N-terminal protein sequence analysis for 25 amino acids above the 500-fmol scale ranged from $50 to $1650, with an average cost of $505. This wide variation undoubtedly reflects the percent of costs that each facility must recover.

The charges for synthesizing peptides and oligonucleotides have decreased considerably from 1992 prices, when the average charge to synthesize a 25-mer peptide was $978 and the average charge for a 25-mer oligonucleotide was $93. The charges, however, for sequencing proteins by Edman chemistry have not changed significantly; the 1992 average charge to sequence 25 amino acids was $427.

Several facilities reported charging higher rates for outside users. Nonprofit facilities charged on average 60% more for outside users, and for-profit facilities charged 91% more. This latter figure is a significant drop ($P < 0.005$) from the additional 159%

TABLE 9

Cost Recovery for Services

Service	Cost Recovery (%)				
	N	Median	Mean	SD	Range
DNA services					
DNA synthesis 1–4	24	95	85	27	21–150
DNA synthesis high	6	80	80	17	60–100
DNA oligo purification	11	100	94	24	60–150
DNA sequencing	25	100	88	25	20–150
Microsatellite analysis	9	70	63	34	10–100
Protein services					
N-terminal protein seq	41	50	59	32	5–115
SDS PAGE	10	63	63	42	5–120
2D gels	8	50	52	33	5–100
Fragmentation	26	50	57	32	5–120
Peptide synthesis 1–3	29	75	67	33	40–120
Peptide synthesis high	9	70	71	27	30–100
Peptide purification	24	90	79	31	10–140
Amino acid analysis	25	65	67	32	8–120
CE	7	50	55	35	20–100
HPLC	16	100	85	50	1–230
Mass spectrometry					
MALDI (mass)	19	60	61	36	5–100
MALDI (sequence)	4	62	59	38	10–100
Electrospray (mass)	11	30	35	29	5–100
Electrospray triple quad	8	50	53	36	8–100

reported by for-profit users in 1992. On the extreme, in 1998 some facilities reported charging as high as three times the in-house rate.

How well each service provided cost recovery, including staff salaries, instrument maintenance, and depreciation and reagent costs, for that service is reported in Table 9. A cluster of services (ie, DNA synthesis, DNA purification, DNA sequencing, HPLC, and synthetic peptide purification) all reported an average of 80% to 100% cost recovery. The lowest average cost recovery value was reported for electrospray (mass) mass spectrometry (35%). For each service at least one laboratory reported that they recovered 100% of the cost of performing that service.

Using sample through-put data and charges provided by each laboratory, we calculated the expected user fee income for each laboratory. From this calculation, we found that user income data provided by respondents averaged 72% ± 57% of the calculated value (median, 69%; range, 0.7% to 207%), suggesting that a number of samples are processed by a laboratory for control purposes, and these do not generate income.

CONCLUSIONS

Biotechnology core laboratories continue to service the research community with a variety of protein and DNA services required for advances in proteomics and genomics. Except for a few laboratories that are totally self-sufficient, core facilities for the most part continue to be subsidized as reflected in the range (35% to 94%) of average cost recovery for services. In return, researchers obtain highly skilled services, with relatively quick turnaround times. Far from being static, the modern facility continues to add new services. For example, in the past 5 years, 2D gel electrophoresis, microsatellite analysis, C-terminal protein sequencing, and all aspects of mass spectrometry have appeared in several facilities. Upcoming services include optical biosensors, gene chip microarray technology, and quantitation by real time PCR. A few laboratories are offering analytical services at the GLP level. This will be an important trend to follow into the future.

The modern biotechnology core facility continues to offer selected services from a set of standard

services. These include N-terminal protein sequencing, fragmentation of proteins for internal sequencing, amino acid analysis, peptide synthesis, HPLC separation of proteins and fragments, DNA synthesis, and DNA sequencing. These standard services were also available at biotechnology core facilities in 1992, when the previous survey was conducted.

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